

REMARKS/ARGUMENTS

Claims 1, 3, 5-7, 11, 12 and 19 were pending in the instant application. The following remarks, in conjunction with the above amendments, are believed to be fully responsive to the Office Action.

THE REJECTIONS UNDER 35 U.S.C. § 103

SHOULD BE WITHDRAWN

Claims 1, 3, 5-7, 11, 12 and 19 stand rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 6,033,645 ("Unger"). In response, Applicants submit that each of the rejections should be withdrawn.

Examiner asserts on page 6, last paragraph that [T]he rates of infusion of Unger fall within the scope of the instant limitation of claim 1, "controllably", because it falls within the ranges that are described by Unger (see col. 44-47). Examiner further asserts that [U]nger claims delivery of his contrast agent in a continuous infusion (col. 64, lines 20-29).

Applicant note that the reference to "continuous infusion" in Unger relies on col. 64, lines 20-29 in US patent 6,033,645 which corresponds to claim 209. Applicant has thoroughly studies the specification of the US patent and also the corresponding International Patent Application published as WO 97/48337 on 24th December 1997. The terms "infusion" or "continuous infusion" is not found in the specification and the claims of WO 97/48337 and also not in the specification of US patent 6,033,645. Hence, the mention of "continuous infusion" was first published on 7th March 2000 which is the publication date of the cited US patent. The instant application claims priority from 27th August 1999, GB 9920392. Applicant therefore holds that US patent 6,033,645 is not valid as §103a prior art with regard to the features related to "infusion" in the instant claims.

Applicant respectfully submits that the objections cited above should therefore be withdrawn. Examiner further holds that [T]he position of the syringe carrying the contrast agent in Unger is vertical (see figure 1).

Applicant has carefully studied Figure 1 of Unger. In applicant's opinion it is impossible to determine from Figure 1 the position of the syringe 20. The syringe may be in vertical or horizontal position depending on how the 2-dimensional drawing is viewed in the 3-dimensional room. However, it is clear from Figure 1 and col 49, lines 65 – 67 that the tubing (30) and the needle (32) are positioned lower than the syringe (14). In Figure 2 it is for the same reasons impossible to determine if the syringe 14 is meant to be positioned in a particular horizontal or vertical position or in a position having a specific position between these two extremes. Unger in the specification does not discuss the positioning of the syringe, whether it should be positioned vertically, horizontally or in a position between these extremes.

Instant claim 1 reads on that the gas-containing contrast agent is delivered from an upper extremity of an essentially vertically position syringe. Applicant respectfully submits that this step that is not taught by Unger and that Unger does therefore not teach all elemental steps of the instant claims.

Applicant respectfully requests that the objections cited above should therefore be withdrawn.

Examiner asserts on page 7, 2nd paragraph that [T]he flushing step of Unger allows complete transport of the gaseous contrast agent into the bloodstream; thus at least a portion of the contrast agent of Unger is mixed with the flushing agent of Unger prior to the administration into the subject (col 47, lines 60 – col 48, line 10).

Applicant has carefully reread in US patent 6,033,645 and disagrees that there are any reference whatsoever that can be interpreted to indicate that at least a portion of the contrast agent of Unger is mixed with the flushing agent of Unger prior to the administration into the subject.

To the contrary, in col. 47, line 60 – col. 48, line 10, Unger notes that the injected lipid and/or vesicle composition may pool or accumulate at or near the site of injection. This clearly tells that the lipid and/or vesicle composition is injected first and is inside the blood vessel before the flush is administered. Unger further holds as the next step, in order to promote the transport of the lipid and/or vesicle from the injection site into the bloodstream and, thereafter, to the region of interest, a flush may be administered. This again clearly tells that the composition is injected into the subject as a first step, and is transported from the injection site by providing a flush. For diagnostic ultrasound of myocardial tissue with a contrast agent that comprises lipid and/or vesicle composition, Unger holds that a flush may be administered after injection of the lipid and or vesicle composition. Thus, Unger makes it clear that the composition is first injected into the body and after the composition is injected, thereafter a flush may be administered.

Hence, there is no mention whatsoever that Unger teaches that not even a portion of the composition is intended to mix with the flushing agent prior to the administration into the subject.

Applicant therefore submits that the step in the instant claim 1 reading on [d]elivering said gas-containing contrast agent from an upper extremity of an essentially vertical positioned syringe and admixing with a flushing agent prior to the administration to the subject is not obvious from Unger. There is no indication in Unger that admixing before administration was intended. To the contrary, since Unger states that the flush is administered after the injection of the composition, the skilled artisan would have no motivation to derive from this procedure.

Applicant therefore submits that claim 1 contain a step, the admixing step, that is not a step taught by Unger and that Unger does not teach all elemental steps of the instant claims.

Applicant respectfully requests that the objections cited above should therefore be withdrawn.

Examiner asserts that [E]ven though, Unger fails to explicitly recite the instantly claimed infusion period of 5-60 minutes, he explicitly places one of ordinary skill in the art at notice that the rate of administration can be optimized based on the volume of the composition, gaseous vesicles, type of encapsulation and other patient variable such as age, are of interest etc.

Applicant submits, see the arguments above, that Unger fails to teach “infusion” in a document that can be held as valid prior art against the instant application since the term “infusion” is only disclosed in the claims of US patent 6,033,645 which is published after the priority date of the instant application.

Examiner further asserts that [S]ubsequently, absent of a showing of unexpected results, it would have been obvious to one of ordinary skill in the art at the time of invention to optimize the rate of administration of the contrast agent of Unger by routine experimentations and enhance the quality of the images, because Unger explicitly recite the rate dependent factors.

Applicant draws Examiner’s attention to Figure 3 of the instant application. Figure 3 depicts the results of the in vivo experiments referred in Example 15 of instant application where images were recorded following the injection of an bolus of contrast agents as prepared in Preparation 1 at a concentration of 30 nl/perfluorobutane/kg and during infusion of contrast agent in accordance with the method of the invention at rates corresponding to 5, 15, 45 and 135 nl/perfluorobutane/kg. It should be noted that the infusion agent is admixed

with the flushing medium. Figure 3 clearly demonstrate the benefit of the infusion of the bubbles admixed with the flushing medium in comparison with the bolus injection, and showed that the infusion unexpectedly provides a considerably higher and longer lasting contrast enhancement.

Applicant respectfully requests that the objections cited above should therefore be withdrawn.

CONCLUSION

In view of the amendments and remarks herein, applicants believe that each ground for rejection or objection made in the instant application has been successfully overcome or obviated, and that all the pending claims are in condition for allowance. Withdrawal of the Examiner's rejections and objections, and allowance of the current application are respectfully requested.

The Examiner is invited to telephone the undersigned in order to resolve any issues that might arise and to promote the efficient examination of the current application.

Respectfully submitted,

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